

REMARKS

Applicants respectfully request reconsideration of this application in view of the above amendments and the following remarks.

1. Status of the Claims

Claims 40-64 are presently pending in the application.

In the present amendments, Claims 40-55 and 58-61 have been canceled and Claims 56, 57, 62, and 63 have been amended. Upon entry of the above amendments, Claims 56-57 and 62-64 remain pending for examination on the merits.

2. Amendments to the Claims

Claims 40-55 and 58-61 have been canceled without prejudice or disclaimer. Applicants specifically reserve the right to file a continuation or divisional application (as appropriate) directed to the subject matter of these claims.

Claim 56 has been amended to be an independent claim, and to define all of the variables of formula (XX). Support for this amendment can be found, for example, on page 48, line 29, through page 49, line 14 of the specification as filed; and original Claims 5, 25, and 33.

Claim 57 has been amended to delete compounds 29-31, 36 and 37.

Claims 62 and 63 have been amended to depend from Claim 56.

No new matter has been added.

Entry of the above amendments is respectfully requested.

3. Rejections under 35 U.S.C. §102(b)

Anticipation under 35 U.S.C. §102 requires that each and every element of the claimed invention be disclosed in a prior art reference. A reference that merely discloses similar but not identical elements is insufficient to anticipate the claimed invention.

3a. Lacefield et al. (GB 1,584,428)

Claims 40-47, 51, 52, and 54 have been rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Lacefield et al.

In view of the cancellation of Claims 40-47 51, 52 and 54, this rejection may be withdrawn.

3b. Werner, US 3,449,418 (Werner)

Claims 40-45, 48, 53, 56, and 61-63 have been rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Werner, US 3,449,418. For the following reasons, this rejection is respectfully traversed.

Claims 40-45, 48, 53, and 61 have been canceled, therefore this aspect of the rejection is moot.

Applicants have focused the claims on compounds having specific features. Amended Claim 56 (and Claims 62-63 which depend therefrom) is to compounds of formula XX, wherein: (a) Y is -NH₂; (b) the phenylene rings are di-substituted with methyl or chloro at the 3 and 5 position relative to Q on the phenylene ring; and (c) Q is methylene.

In contrast, the compounds disclosed in Werner differ in at least two aspects from Applicants' compounds of amended Claim 56. In the compounds disclosed in Werner, the amino groups are always dialkylamino; and the phenylene rings are always di-substituted with at least one tertiary alkyl when Werner's compounds have a methylene bis(phenoxy) core. Since Werner does not teach each and every limitation of the present claims, Werner does not anticipate the present invention.

Accordingly, Applicants respectfully request that the rejection of Claims 40-45, 48, 53, and 61-63 under 35 U.S.C. §102(b) as being anticipated by Werner, US 3,449,418, be withdrawn.

3c. Wegler, DE 1 218 039

Claims 40-43, 45-48, 51, 52, 53, and 55 have been rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Wegler et al., DE 1 219 039.

Claims 40-43, 45-48, 51, 52, 53, and 55 have been canceled, therefore this rejection may be withdrawn.

3d. Benoit et al., Chem. Abst. 47:12092

Claims 40, 42-43, 45-46, 53, 61, and 62 have been rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Benoit et al., Chem. Abst. 47:12092.

Claims 40, 42-43, 45-46, 53, and 61 have been canceled, therefore this aspect of the rejection is moot.

Claim 62 has been amended to depend from Claim 56, which was not rejected.

Therefore Applicants respectfully request that the rejection of Claims 40, 42-43, 45-46, 53, 61, and 62 under 35 U.S.C. §102(b) as being allegedly anticipated by Benoit et al. be withdrawn.

4. Rejections under 35 U.S.C. §103(a)

4a. Wegler et al., DE 1,219,039

Claims 40-44 and 49-55 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Wegler et al. (DE 1,219,039).

In view of the cancellation of Claims 40-44 and 49-55, this rejection may be withdrawn.

4b. Lacefield et al. (GB 1,584,428)

Claims 40-49, 51, 52, 54, 58 and 59 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Lacefield et al. (GB 1,584,428).

In view of the cancellation of Claims 40-49, 51, 52, 54, 58 and 59, this rejection may be withdrawn.

4c. Lowe et al., Chem. Abst., 46:48437

Claims 40, 42-44, 46, 48-49, 52, 61-63 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Lowe et al.

Claims 62 and 63 have been amended to depend from Claim 56, which was not rejected.

Claims 40, 42-44, 46, 48-49, 52, and 61 have been canceled, thus rendering this aspect of the rejection moot.

Therefore, Applicants respectfully request that the rejection of Claims 40, 42-44, 46, 48-49, 52, 61-63 under 35 U.S.C. §103(a) as allegedly being unpatentable over Lowe et al. be withdrawn.

4d. Werner (US 3,449,418) and Benoit et al. (Chem Abst. 47:12092), taken with Marxer et al. (US 3,247,199) and Rafferty et al. (US 5,736,568)

Claims 40-64 have been rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over the combined teachings of Werner (US 3,449,418) and Benoit et al. (Chem Abst. 47:12092), taken with Marxer et al. (US 3,247,199) and Rafferty et al. (US 5,736,568).

For the following reasons, Applicants respectfully traverse the rejection on the grounds that the Examiner has not established a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, the Examiner must make three showings:

(1) First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references in a manner that produces the claimed invention. *See, In re Fine*, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

(2) Second, the Examiner must show that the proposed modification of the prior art references had a reasonable expectation of success as determined from the vantage point of one of ordinary skill in the art. *See Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343, 56 USPQ2d 1641, 1644 (Fed. Cir. 2000). Both the motivation to modify the prior art references, as well as the expectation of success, must come from the prior art; not from applicant's own disclosure. *See, In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

(3) Lastly, the Examiner must show that the prior art reference or combination of references teach or suggest all the limitations of the claims. *See, In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

If the Examiner fails in any of these requirements, he has not established a *prima facie* case of obviousness, and without more, the applicant is entitled to a patent. *See, e.g., Oetiker*, 977 F.2d at 1445, 24 USPQ2d at 1444 (citing *In re Grabiak*, 769 F.2d 729, 733, 226 USPQ 870, 873 (Fed. Cir. 1985)).

Serial No. 10/824,738
Attorney Docket No.: P-097-US2
Amendment and Response

Page 8 of 12

In the present amendment, Applicants have focused the claims on compounds of formula XX, wherein: (a) Y is -NH₂; (b) the phenylene rings are di-substituted with methyl or chloro at the 3 and 5 position relative to Q on the phenylene ring; and (c) Q is methylene.

In view of the newly focused claims, the Examiner has not provided a sufficient explanation of why one of ordinary skill in the art would have been motivated to modify the teachings of each of the cited references in very specific ways at multiple positions to arrive at the presently claimed invention. Without a sufficient explanation of why one of ordinary skill in the art would have been motivated to make the specific compounds of the present invention, the Examiner has not established a *prima facie* case of obviousness.

Werner, US 3,449,418 (Werner)

All of Werner's exemplified compounds, whether of Werner's formulae I, II, or III, differ structurally in at least two aspects from Applicants' claimed compounds of formula XX. In the compounds disclosed in Werner, the amino groups are always dialkylamino; and the phenylene rings are always di-substituted with at least one tertiary alkyl when Werner's compounds have a methylene bis(phenoxy) core.

Further, there is no motivation or reasonable expectation of success for one skilled in the art to modify Werner's teachings of anti-inflammatory, antibacteriacidal, and antiparasitic compounds in order to arrive at Applicants' compounds of formula XX, which function as sodium channel modulators to control pain.

Benoit et al., Chem. Abst. 47:12092 (Benoit)

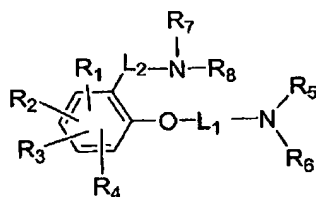
Structurally Benoit's compounds differ in at least two aspects from Applicants claimed compounds of formula XX. Benoit's compounds only have dialkylamino groups (whereas Applicants' structure has only -NH₂ groups); and Benoit's compounds always have unsubstituted phenyl rings (whereas for Applicants' compounds of formula XX, the phenyl rings are di-substituted with methyl or chloro at fixed positions).

One skilled in the art would not have been motivated based on the teachings of Benoit to make the multiple modifications to Benoit's compounds that would have been required to provide Applicants' compounds of formula XX.

The combined teachings of Werner (U.S. 3,449, 418), and Benoit et al. (Chem. Abst. 47:12092) do not provide any motivation for one skilled in the arts to make multiple modifications to Benoit's and/or Werner's compounds that would have been required in order to achieve Applicants' compounds of formula XX. Further, the combined teachings of the two references which disclose antibacteriacidal and anti-inflammatory compounds would not motivate one skilled in the art in the making of compounds that function as sodium channel modulators, such as Applicants' claimed invention.

Rafferty et al., U.S. 5,736,568 (Rafferty)

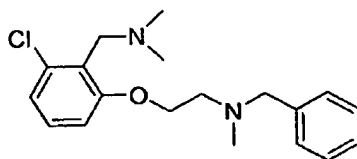
Rafferty's compounds are structurally very different from Applicants' claimed compounds. Rafferty discloses anti-inflammatory compounds useful in the treatment of asthma of the following structure:



Rafferty, formula I

wherein L₁ and L₂ are alkylene chains.

To make the comparison clearer, Rafferty's Example 1, 2-[2-N-benzyl-N-methylamino)ethoxy]-6-chloro-N,N-dimethylbenzylamine, (Col. 25, lines 5-50), typical of Rafferty's compounds, is drawn below for the Examiner's convenience:



Rafferty, Example 1

Rafferty's compounds differ in multiple aspects from Applicants' compounds of formula XX in that Rafferty's structures (1) do not have a central methylene bis(phenyloxy)core; (2) lack a second phenoxy group; (3) the oxygen atom and L₂ group are positionally *ortho* on the phenylene ring (as compared to Applicants' compounds of formula XX, in which the oxygen atom is positionally *para* to a central methylene core); and (4) in Rafferty's 39 examples, no compounds are disclosed with two primary amino groups.

Given that Rafferty's compounds are also structurally different from Werner and Benoit's disclosed compounds in multiple aspects (Rafferty's compounds do not have a central methylene bis(phenyloxy)core; and lack a second phenoxy group), it is not clear how to apply Rafferty's teachings to Werner and Benoit's compounds. Further, based on Rafferty's disclosure, one skilled in the art would not be motivated to modify Werner's and/or Benoit's compounds in the necessary multiple places in order to achieve Applicants' claimed compounds of formula XX.

Marxer et al., U.S. 3,247,199 (Marxer)

Marxer's compounds differ in at least two aspects from Applicants' compounds of formula XX: (a) Marxer's core methylene is always di-substituted with alkyl groups which optionally form a ring; and (b) Marxer's structures have di-alkyl amino groups, which optionally form heterocycles. Marxer does not teach Applicants' compounds of formula XX wherein Q is methylene, and Y is -NH₂.

Marxer teaches that his compounds display an antipyretic, analgesic and anti-inflammatory action, as noted in the Office Action. However, Marxer does not provide any details as to how the pharmacological properties of his compounds were demonstrated, or provide any comparative data as to how to modify the structural features of a compound to improve its analgesic efficacy. Thus, for one skilled in the art, the Marxer reference does not provide any motivation or suggestion as to how to modify Rafferty, Werner and/or Benoit's compounds to make the specific compounds of Applicants' instant claims.

The cited references, either alone or in combination with each other do not teach or suggest all the limitations of the Applicants' presently pending claims to compounds of formula XX, wherein Q is methylene, the phenylene rings are di-substituted with methyl or chloro at the 3 and 5 position relative to Q on the phenylene ring, and Y is -NH₂.

It is well established that the Examiner is not permitted to use hindsight to pick and choose variables to arrive at Applicants invention without some motivation in the prior art to select particular variables in preference to other possible selections. Some motivation to select the claimed species must be taught by the prior art. The fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness (*In re Baird*, 16 F.3d 380,382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994). See MPEP § 2144.08(II)(A)(4)(a); and *In re Duell*, 51 F.3d 1152, 1558, 34 USPQ2d 1210, 1215.

In this regard, Applicants respectfully submit that, in the absence of hindsight knowledge of Applicants' presently claimed invention, there is nothing in the disclosure of Marxer, Rafferty, Benoit, and Werner to provide the requisite motivation to modify such teachings in a manner that would result in Applicant's presently claimed compounds. Without such specific motivation, a *prima facie* case of obviousness cannot be properly established.

For the foregoing reasons, Applicants respectfully request that the rejection of Claims 40-64 under 35 U.S.C. 103(a) as being allegedly unpatentable over the combined teachings of Werner and Benoit et al., taken with Marxer et al. and Rafferty et al., be withdrawn.

5. Conclusion

Applicants have amended the claims such that upon entry of the above amendments, Claims 56-57 and 62-64 remain pending for examination on the merits.

Applicants believe that this application is now in condition for allowance. Should there be any remaining issues that can be resolved by telephone, the Examiner is respectfully requested to telephone the undersigned agent at (650) 808-6144.

Respectfully submitted,
THERAVANCE, INC.

Date: April 3, 2006

By: Joyce G. Cohen
Joyce G. Cohen, Reg. No. 44,622

THERAVANCE, INC.
901 Gateway Boulevard
South San Francisco, CA 94080
Phone: (650) 808-6000 Fax: (650)-808-6078
Phone: (650) 808-6144 (direct)